REMARKS

Amendment and Status of the Claims

Claims 62, 70, 71, 76-80, and 82-84 have been amended to correct minor informalities, to more particularly point out and distinctly claim certain subject matter, and/or to provide appropriate dependency. No new matter has been added.

Claims 64 and 85 have been cancelled without prejudice or disclaimer.

Now pending in the application are claims 62-63, 66, 69-80, and 82-84.

As an initial matter, Applicant points out that claim 62 (from which the remaining method claims depend), as now pending, is directed to a method of treating premature ejaculation in a male consisting of administering to the male an antidepressant via a combination of nasal administration and local administration to at least a part of the male genitalia

Applicant notes with appreciation that the previous rejection under 35 U.S.C. §112, second paragraph has been withdrawn.

Rejection under 35 U.S.C. §103(a)

Claims 62-64, 66, 69-80 and 82-85 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Crenshaw et al. (U.S. Patent No. 5,151,448) and Choi et al. (U.S. Patent No. 5,587,167), in view of Smith et al. (U.S. Patent No. 5,922,341) and El-Rashidy (U.S. Patent No. 5,256,167). This rejection is traversed.

Crenshaw teaches that premature ejaculation in male humans patients can be effectively treated by the administration, preferably oral, of a fluoxetine dose effective to delay the onset of ejaculation during subsequent sexual intercourse (see, e.g., column 1, lines 49-52). As recited again at column 1, lines 59 and 59, oral administration is preferred.

Although Crenshaw discloses that other routes of administration e.g., parental, by suppositories, buccal dosage forms, skin patch, and the like, can also be utilized (see, e.g., column 2 lines 66-68), the skilled artisan is directed to administer fluoxetine

by oral administration. As taught by Crenshaw et al., at column 2, line 68 to column 3, line 8:

> The active ingredient in the individual dosage forms can be combined with the conventional pharmaceutical excipients and formed into tablets, capsules, and the like. Tablets may be scored for divided dosage administration. Alternatively, the active ingredient may be dissolved in a suitable liquid vehicle such as water, fruit juice, or the like. For chronic administration of the active ingredient oral dosage forms are preferred.

Crenshaw does not teach administration of an antidepressant by nasal administration, nor does it teach the combination of nasal administration and local administration to at least part of the male genitalia, as presently claimed (and as the Office Action appears to concede). Indeed, Crenshaw does not teach any form of administration other than administration via a single route, in which administration is preferably oral administration.

The Examiner asserts that Choi teaches that a formulation may be administered locally (topically) to a part of the male genitalia for premature ejaculation (Office Action at page 10). Applicant respectfully contends that the teachings of Choi cannot be combined with the teachings of Crenshaw as asserted in the Office Action. Choi teaches the use of a galenic composition for the prophylaxis and treatment of male ejaculation accommodation ataxia (column 1, lines 17-18), in contrast to the present invention, in which antidepressants are used. Moreover, Choi teaches that, in their clinical test, the patient was instructed to uniformly apply the ointment (galenic composition) to the penis glans in an amount of 0.2 g each time sexual intercourse was anticipated. Then the ointment was to be washed off after 20 to 30 minutes. Thus, Choi is directed to galenic compositions which are removed 20 to 30 minutes after application. The combination of the teachings of Choi with the teachings of Crenshaw is improper; the references teach different compositions and methods that cannot properly be combined in this way.

The Office Action states that Smith teaches that a "pharmaceutical composition[ ] . . . may also be administered by nasal aerosol or inhalation." However, Smith discloses that the administration of fluoxetine has many undesired aspects (column 1, lines 51-67). Thus, Smith teaches a method for treating premature ejaculation by

administering an effective amount of a serotonin antagonist or agonist (column 2, lines 61-63). Moreover, Smith teaches administering the serotonin antagonist or agonist via a single route of administration, e.g., transurethrally or via intracavernosal injection (column 2, line 55 to column 3, line 27). Smith is completely silent as to a method of administering an antidepressant to a patient via a combination of two independent routes for treating premature ejaculation in a male.

Smith teaches that the preferred mode of administration is transurethrally (see abstract). Smith teaches that it may be desirable to deliver the active agent in a urethral dosage form which provides for controlled or sustained release of the agent. To effect the administration, Smith teaches the use of a transurethral inserter as depicted in Figure 1 thereof. As disclosed in Examples 1-4, Smith teaches that a pharmaceutical formulation for transurethral administration is prepared comprising a serotonin or adrenergic antagonist or agonist in a suppository form. Thus, Smith *et al.* teaches away from the present invention. Smith is also silent as to the administration of an antidepressant via a combination of nasal administration and local administration to at least part of the male genitalia. Smith also does not teach a kit which can achieve the same. Further, the transurethral application method required by Smith is unlikely to suggest alternative administration routes. One of ordinary skill in the art would consider that if such a transurethral route is specified, it is because it was the only available and realistic route to achieve the desired effect.

The Examiner states that El-Rashidy teaches methods for treating premature ejaculation in which HPBCD may be administered in a ratio that is the same ratio as disclosed in the present claims (Office Action at page 10). However, El-Rashidy discloses the use of a peripheral vasodilator and hydroxypropyl-cyclodextrin (see column 3, lines 10 to 14). According to the present claims, an antidepressant is used as the active agent, not the peripheral vasodilator papaverine as disclosed by El-Rashidy. El-Rashidy does not teach or suggest that hydroxypropyl-cyclodextrin would be useful in a method using an antidepressant as the active agent. Furthermore, El-Rashidy discloses a topical composition which enhances the maintenance of penile erection, as opposed to the treatment of premature ejaculation. Contrary to statements in the Office Action, El-Rashidy does not necessarily teach or suggest the use of

HPBCD with an antidepressant for the treatment of premature ejaculation in the desired ratio; in fact, El-Rashidy teaches the presence of a peripheral vasodilator for maintenance of penile erection.

Thus, none of the references, taken alone or in any combination, can render obvious the claimed subject matter.

As Applicant has previously discussed, the present invention is directed towards the administration of an antidepressant via a combination of nasal administration and administration to at least a part of the male genitalia to significantly improve the time to ejaculation, which is otherwise not achievable when the antidepressant is administered via only one route of administration.

As disclosed in the present specification, the Applicant has surprisingly found that by splitting the routes of administration, an increased level of satisfaction is experienced by patients suffering from premature ejaculation. The symbol ++ in the table at page 15 of the specification relates to a measure of satisfaction, which is not a quantitative measure. It is believed (without wishing to be bound by theory), based upon clinical observation, that by splitting the routes of administration, the medicament can absorb rapidly into the central nervous system and, at the same time, act on the nerve endings in the penis to provide partial desensitization. This effect is otherwise not achievable if the antidepressant is administered via only one route. This is neither taught nor disclosed in the cited prior art. This effect is also unexpected and unpredictable.

None of the prior art citations teach nor disclose a method or medicament for the treatment of premature ejaculation consisting of an antidepressant formulated for nasal administration and an antidepressant formulated for local administration to at least part of the male genitalia. Although the Office Action asserts that it is known that "in order to maximize therapeutic efficacy, more than one mode of administration would be necessary in order to achieve optimal therapeutic efficacy as an added measure," Applicant respectfully submits that without any positive indication to do so, one of ordinary skilled in the art would not employ more than one route of administration when the prior art is replete with teachings of single route administration. The cited prior art does not teach the person skilled in the art to administer an antidepressant specifically

via a combination of nasal administration and local administration to at least a part of the male genitalia with the expectation that this would lead to an improvement in time to ejaculation, and result in an increased level of satisfaction when compared with that experienced through single route administration. Moreover, as discussed above, the claimed methods and medicaments provide unexpected and superior results compared to single-route methods of administration.

None of the cited references teaches or discloses, either alone or in any combination, a method of treating premature ejaculation in a male comprising administering to the male an antidepressant via a combination of mucosal administration and local administration to at least a part of the male genitalia, as claimed in pending claim 62 (and claims dependent therefrom). The cited references also neither teach nor disclose, either solely or collectively, a composition for the treatment of premature ejaculation comprising an antidepressant formulated for mucosal administration and for local administration to at least a part of the male genitalia, as claimed in pending claim 76 (and claims dependent therefrom), nor a kit comprising an antidepressant formulated for nasal administration and an antidepressant formulated for local administration to at least part of the male genitalia, as claimed in pending claim 85.

Reconsideration and withdrawal of the rejections is proper and the same is requested.

Supplemental Information Disclosure Statement

The Examiner's attention is directed to the Supplemental Information Disclosure Statement (IDS) filed on February 12, 2009, in connection with the present application. Applicant requests that the Examiner consider the references cited and return an initialed copy of the IDS to Applicant with the next Office Action or Notice of Allowance.

CONCLUSION

For at least the foregoing reasons, all claims of this application are deemed to be in condition for allowance, and allowance is accordingly requested. However, if the

Examiner considers that obstacles to allowance remain, the Examiner is invited to contact the undersigned.

Applicant requests any extension of time necessary for consideration of this response. If for any reason a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, you are hereby authorized and requested to charge Deposit Account No. **04-1105**, under Reference No. 64734 (70403), Customer No. 21874.

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Respectfully submitted,

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